UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/647,789	08/25/2003	Daniel P. Wermeling	INT-001 B	2016

51414 7590 11/30/2009

GOODWIN PROCTER LLP
PATENT ADMINISTRATOR
53 STATE STREET
EXCHANGE PLACE
BOSTON, MA 02109-2881

EXAMINER	
BETTON, TIMOTHY E	

ART UNIT	PAPER NUMBER
1627	

NOTIFICATION DATE	DELIVERY MODE
11/30/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PatentBos@goodwinprocter.com
hmcpeake@goodwinprocter.com
glenn.williams@goodwinprocter.com

Office Action Summary	Application No.	Applicant(s)	
	10/647,789	WERMELING, DANIEL P.	
	Examiner	Art Unit	
	TIMOTHY E. BETTON	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,10-13,16-20,46-67 and 70-72* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *53-67 and 70-72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 16 October 2009 has been entered.

Status of the Claims

Claims 5-6, 9, 14-15, 21-45, and 68-69 are cancelled. Claims 1-4, 7-8, 10-13, 16-20 and 46-52 are withdrawn from further consideration. Claims 53-67 and 70-72 are pending further prosecution on the merits.

Formal Matters

Upon further consideration of the Bibliography Data sheet dated 19 October 2009, the limitation drawn to preservative-free does not get the filing date of 5/10/2000 attributed to application 09/569125. Nor does the limitation get the filing date of the USPN 6,610,271 because neither the application nor patent aforementioned disclose the limitation drawn to preservative-free. The claim set submitted 25 August 2003 is recorded as the initial claim set to include the limitation, "preservative free". Thus, the limitation “preservative-free" gets the filing date of 25 August 2003 instead of 10 May 2000 or 20 February 2001.

Response to Arguments

Applicants Remarks filed on 16 October 2009 have been acknowledged and duly made of record.

Applicant's arguments see Remarks, filed 16 October 2009, with respect to *35 U.S.C. § 103(a)* rejection have been fully considered and are persuasive. The previous 103(a) rejection of 16 April 2009 has been withdrawn.

Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections- 35 U.S.C. 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 53-59 and 62-67, 70, and 71 are rejected under 35 U.S.C. 103(a) as being unpatentable over Levin, B. (PGPUB US 2001/0004644 A1) and Hansen et al. (USPN 5,179,079) in view of Aliverti et al., (USPN 5,183,802), Midha (USPN 6,127,385), and Shahinian (USPGPUB 2002/0061340).

Levin teaches methods comprising intranasally administering to the patient a pharmaceutical composition comprising a local anesthetic. Levin further discloses butorphanol

tartrate for use in intranasal device for muscular headaches (page 2, section [0018]; page 21, section [0200]; page 39, claim 24).

Levin teaches administration of butorphanol tartrate aqueous formulation in an intranasal device which is obvious over instant claim 53 which teaches a pharmaceutical composition comprising an effective amount of an opioid.

Levin does not teach a buffering agent, aqueous diluent, masking agent or sucrose to be administered in the intranasal formulation.

However, Hansen et al. resolves the deficiency in Levin by teaching in column 4 at lines 8-29, [t]he preparation of this invention may be liquid, e.g. adapted for administration as a spray or a solid, e.g. a powder acceptable for snuffing. Liquid preparations, such as those based on aqueous formulations, will usually include ancillary agents, for example a pH-buffering system, preferably a buffer such as **phosphate, citrate or acetate buffers**, a preservative and an osmotic pressure controlling agent, e.g. glycerol or sodium chloride. Powder formulations may contain the pharmaceutically active agent and the absorption enhancing system in admixture with nasally acceptable powdery diluents or mixtures thereof, e.g. cellulose or derivatives thereof, for example cellulose ethers or sodium carboxymethylcellulose, starch, a long chain fatty acid or a salt thereof, e.g. aluminum stearate, an organic polymer, e.g. of an acrylic acid derivative or inorganic vehicles, such as talc or diatomaceous earth. Supplementary addition of water-absorbing polymers, for example polyethylene glycol or polyvinyl pyrrolidone may be desirable to improve adhesion of the powder formulation to the nasal mucosa.

Further, Hansen et al. meets the limitation in the claims drawn to an aqueous diluent by teaching water in column 4 at lines 30-31.

Still further, Hansen et al. is obvious over the scope and content of the claimed invention by teaching in column 5 at lines 35-44 that [t]he preparations of this invention may be used in any dosage dispensing devices adapted for intranasal administration. The devices should be constructed with a view to ascertaining optimum metering accuracy and compatibility of its constructive elements, such as container, valve and actuator with the nasal formulation and could be based on a mechanical pump system, e.g. that of a metered-dose nebulizer, or on a pressurized aerosol system.

Hansen et al. does not teach sucrose.

However, Aliverti et al. resolves the deficiency in Hansen et al. by teaching intranasal formulations containing sucrose in column 16 at lines 60-61, Table 19 at line 54 (specifically) in a suitable intranasal formulation.

The mere propensity that sucrose would be incorporated into a nasal formulation reasonably suggests that this component would reasonably be incorporated into the nasal formulation of the claimed invention. The fact that Hansen contemplates and discloses this component in an intranasal formulation regardless of the active ingredient sufficiently suggests obviousness over the claimed invention in view of claim 72.

The formulations of Examples 53 and 54 are prepared by mixing together the sucrose, the mannitol and the lactose. The resulting mixture is wetted with an aqueous solution of elcatonin, granulated through a stainless steel screen and dried under vacuum. The dried

granules are mixed with ammonium glycyrrhizinate, carbopol and polyethylene glycol and then compressed into tablets of 150 mg each.

Aliverti et al. does not teach a sweetening agent in the intranasal formulation. However, Midha et al. resolves the deficiency in Aliverti by teaching a nasal formulation containing [active agent] dissolved in aqueous or non-aqueous solvent, an antioxidant and aromatic oils as flavoring agents (column 4, lines 59 to 63). In instant claim 61, aromatic oils are disclosed as rosemary oil, spearmint oil, thyme oil, etc. Instant claim 72 specifically discloses sucrose, but Midha et al. does not teach sucrose.

Midha et al. doe not teach the limitation of "preservative-free".

However, Shahinian teaches in the abstract a **self-preserved nasal**, inhalable and topical ophthalmic **preparation and medications which destroy, inhibit or therapeutically significantly limit microbial growth** within said preparations or medications. The nasal, inhalable, and topical ophthalmic preparations and medications are mildly buffered and maintain a stable pH at pH 3.5 or lower.

Shahinian teaches in paragraph 7 that it would be desirable to have available [redacted] preparations and medications suitable for topical, mucosal and inhalation use that could be stored in multi-dose containers without risk of microbial contamination.

Thus, Shanhinian adequately makes the claimed invention obvious by teaching the benefits of a self-preserving nasal formulation in the absence of a well-established preservative BAK.

Thus, it would have been *prima facie* obvious to combine the butorphanol tartrate aqueous formulation of Levin with the intranasal device, buffering agents, aqueous diluents, etc. of Hansen et al. Aliverti et al. is combined with Hansen in obviousness over claim 72 which is drawn to sucrose. Midha provides the motivation based upon the sweetening agent. Shahinian teaches reasoning as to why the one of skill would not incorporate a preservative of any sort into an intranasal formulation. Thus, the scope and content of the claimed invention are suitably made obvious by the references *supra*

The differences in the prior art and the claims at issue are drawn to the limitation in 53 drawn to a preservative-free pharmaceutical composition. As addressed *supra*, applicants' limitation drawn to *preservative-free* is adequately addressed by Shahinian in the absence of the other references addressing the said limitation.

The objective evidence of obviousness is determined to be adequately addressed by Levin, Hansen, and Aliverti teaching inventions directed to intranasal inhibitors. Shahinian overcomes the limitation drawn to preservative-free and explains why it would be beneficial due to the lower incident of toxicity with well-established preservatives. Hansen et al. teach the exemplification of an intranasal device that reasonably encompasses all limitations in the claims drawn to the intended use of an intranasal device as far as optimal actuation. Aliverti et al. contain embodiments drawn to the same aqueous intranasal formulation of Hansen but with sucrose. Thus, objective evidence points ponderously in the direction of obviousness over the claimed invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIMOTHY E. BETTON whose telephone number is (571)272-9922. The examiner can normally be reached on Monday-Friday 8:30a - 5:00p.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

TEB

/Yong S. Chong/
Primary Examiner, Art Unit 1627